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PATENT
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Washington, D.C. 20231

By: _____

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Examiner: Schmidt, M.M.
Barber, et al.	Art Unit: 1635
Application No.:	PRELIMINARY AMENDMENT PURSUANT TO RULE 37 C.F.R. 1.607c.
Filed: February 5, 2002	
For: SUBSTANTIALLY COMPLETE RIBOZYME LIBRARIES	

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

The following amendments and remarks are pursuant to Rule 607(c). This rule provides for the presentation of claims which correspond exactly or substantially to a claim of U.S. Patent No. 6,183,959 ['959] pursuant to 35 U.S.C. §135(b). The amendment is timely as the patent issued on February 6, 2001. Attached to this Amendment is a copy of the '959 patent.

IN THE SPECIFICATION:

On page 1, please delete lines 6 and 7 and replace with:

--This application is a continuation of U.S. patent application 09/357,741, filed July 20, 1999, which is a non-provisional of provisional application 60/093,828, filed July 22, 1998.--

IN THE CLAIMS:

Please add the following new claims 71-100:

--71. A method for identification of a nucleic acid molecule that modulates a process in a biological system comprising the steps of:

a) introducing a random library of a nucleic acid catalyst into said biological system under conditions suitable for modulating said process, wherein said nucleic acid catalyst comprises a substrate binding domain and a catalytic domain, said substrate binding domain comprises a random sequence; and

b) determining the nucleotide sequence of at least a portion of the substrate binding domain of said nucleic acid catalyst from said biological system in which the process has been modulated.

72. A method for identifying one or more nucleic acid molecules involved in a process in a biological system comprising the steps of:

a) providing a library of a nucleic acid catalyst, with a substrate binding domain and a catalytic domain, wherein said substrate binding domain comprises a random sequence, to said biological system under conditions suitable for said process to be altered;

b) identifying any said nucleic acid catalyst present in said biological system where said process has been altered; and

c) determining the nucleotide sequence of at least a portion of the binding domain of said any said nucleic acid catalyst to allow said identification of said nucleic acid molecule involved in said process in said biological system.

73. A method for identification of a nucleic acid catalyst that modulates a process in a biological system comprising the steps of:

a) introducing a random library of a nucleic acid catalyst into said biological system under conditions suitable for modulating said process, wherein said nucleic acid catalyst comprises a substrate binding domain and a catalytic domain, said substrate binding domain comprises a random sequence; and

b) identifying said nucleic acid catalyst from said biological system in which the process has been modulated.

74. The method of any of claims 71-73, wherein said biological system is a bacterial cell.

75. The method of any of claims 71-73, wherein said biological system is of plant origin.

76. The method of any of claims 71-73, wherein said biological system is of mammalian origin.

77. The method of any of claims 71-73, wherein said nucleic acid catalyst is in a hammerhead motif.

78. The method of any of claims 71-73, wherein said nucleic acid catalyst is in a hairpin motif.

79. The method of any of claims 71-73, wherein said nucleic acid catalyst is in a group I intron ribozyme motif, group II intron ribozyme motif, VS ribozyme motif or RNase P ribozyme motif.

80. The method of any of claims 71-73, wherein said process is selected from the group consisting of growth, proliferation, apoptosis, morphology, angiogenesis, differentiation, migration, viral multiplication, drug resistance, signal transduction, cell cycle regulation, temperature sensitivity and chemical sensitivity.

81. The method of any of claims 71-73, wherein said random library of nucleic acid catalysts is encoded by an expression vector in a manner which allows expression of said nucleic acid catalysts.

82. The method of claim 81, wherein said expression vector comprises:

a) a transcription initiation region;

b) a transcription termination region;

c) a sequence encoding at least one said nucleic acid catalyst; and

wherein said sequence is operably linked to said initiation region and said termination region, in a manner which allows expression or delivery or expression and delivery of said nucleic acid catalyst.

83. The method of claim 81, wherein said expression vector comprises:

a) a transcription initiation region;

b) a transcription termination region;

c) an open reading frame for a polypeptide;

d) a sequence encoding at least one said nucleic acid catalyst,

wherein said sequence is operably linked to the 3'-end of said open reading frame; and

wherein said sequence is operably linked to said initiation region, said open reading frame and said termination region, in a manner which allows expression or delivery or expression and delivery of said nucleic acid catalyst.

84. The method of claim 81, wherein said expression vector comprises:

a) a transcription initiation region;

b) a transcription termination region;

c) an intron;

d) a sequence encoding at least one said nucleic acid catalyst; and

wherein said sequence is operably linked to said initiation region, said intron and said termination region, in a manner which allows expression or delivery or expression and delivery of said nucleic acid catalyst.

85. The method of claim 81, wherein said expression vector comprises:

a) a transcription initiation region;

b) a transcription termination region;

c) an intron;

d) an open reading frame for a polypeptide;

e) a sequence encoding at least one said nucleic acid catalyst,

wherein said sequence is operably linked to the 3'-end of said open reading frame; and wherein said sequence is operably linked to said initiation region, said intron, said open reading frame and said termination region, in a manner which allows expression or delivery or expression and delivery of said nucleic acid catalyst.

86. The method of claim 81, wherein said expression vector is derived from a retrovirus.

87. The method of claim 81, wherein said expression vector is derived from an adenovirus.

88. The method of claim 81, wherein said expression vector is derived from an adeno-associated virus.

89. The method of claim 81, wherein said expression vector is derived from an alphavirus.

90. The method of claim 81, wherein said expression vector is derived from a bacterial plasmid.

91. The method of claim 81, wherein said expression vector is operably linked to a RNA polymerase II promoter element.

92. The method of claim 81, wherein said expression vector is operably linked to a RNA polymerase III promoter element.

93. The method of claim 92, wherein said RNA polymerase III promoter is derived from a transfer RNA gene.

94. The method of any of claims 71-73, wherein said biological system is of an eukaryotic origin.

95. The method of any of claims 71-73, wherein said biological system is of a prokaryotic origin.

96. The method of any of claims 71-73, wherein said substrate binding domain is of length between 12 and 100 nucleotides.

97. The method of any of claims 71-73, wherein said substrate binding domain is of length between 14 and 24 nucleotides.

98. The method of any of claims 71-73, wherein said nucleic acid catalyst comprises two substrate binding arms.

99. The method of claim 98, wherein said substrate binding arms are of similar length.

100. The method of claim 98, wherein said substrate binding arms are of different length.--

REMARKS

The Invention.

This invention is the application of catalytic nucleic acid (ribozymes) to effect a phenotypic change in a cell.

Status of the Claims.

Claims 1-70 are pending. New claims 71-100 are added.

Support for the newly added claims.

Claim 71 finds support on page 1, lines 19-20 (describing ribozymes as catalysts) and on page 5 lines 14-25 describing the general method of using ribozymes as tools to effect phenotypic changes. Claim 71 corresponds to claim 1 of the '959 patent.

Claims 72 and 73 also find support in the specification at page 5, lines 14-25. Claims 72 and 73 correspond to claims 2 and 3 of the '959 patent, respectively.

Claims 74-76 find support on page 39, lines 9-10 (bacterial and plant) and on page 41, line 10 (mammalian). Claims 74-76 correspond to claims 4-6 of the '959 patent, respectively.

Claims 77-78, reciting different types of ribozymes, find support on page 1, lines 19-24, and at page 7, line 27. Claims 77-78 correspond to claims 9 and 10 of the '959 patent, respectively.

Claim 79, reciting different types of ribozymes, finds support on page 1, lines 19-24. Claim 79 corresponds to claim 12 of the '959 patent.

Claim 80, reciting different types of phenotypic changes, finds support on page 13, lines 28-35 and on page 46, in the section entitled, "One or more biological activities of the cell...is monitored." Claim 80 corresponds to claim 13 of the '959 patent.

Claims 81-85, reciting different types of expression vectors, find support on page 25 in the section entitled, "Insertion of randomized ribozyme genes into a cloning or expression vector." Claims 81-85 correspond to claims 14-18 of the '959 patent, respectively.

Claims 86-89, reciting different types of viral vectors, find support on page 30 section 4 entitled, "Vectors useful for maximal ribozyme expression." Alphaviruses on page 34, section (c) entitled, "Sindbis/Semliki Forest Virus." Claims 86-89 correspond to claims 19-22 of the '959 patent, respectively.

Claim 90, reciting an expression vector derived from a bacterial plasmid, finds support on the carryover paragraph between pages 25 and 26 where prokaryote expression vectors are described. Claim 90 corresponds to claims 23 of the '959 patent, respectively.

Claims 91-93, reciting different promoters, finds support on page 34, section 4, entitled, "Promoters useful for ribozyme expression." Pol II promoters are mRNA promoters and find support in the Beta-actin and gamma-globin promoter. Claims 91-93 correspond to claims 24-27 of the '959 patent, respectively.

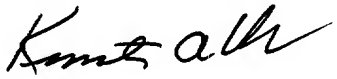
Claims 94-95, reciting biological systems of prokaryotic and eukaryotic origin, find support on page 39, line 10, reciting both prokaryotes and eukaryotes. Claims 94-95 correspond to claims 30-31 of the '959 patent, respectively.

Claim 96, reciting binding domain length, finds support on page 27, line 30. Claim 96 corresponds to claim 33 of the '959 patent.

Claims 97-100, reciting two binding arms, find support on page 1, lines 19-24 describing different ribozymes inherently having two binding arms, and at pages 27-28 describing binding arms. Claims 97-100 correspond to claims 36-38 of the '959 patent, respectively.

Applicants respectfully submit that all of the outstanding concerns raised by the Examiner in the latest action have been fully addressed and that the claims are in condition for allowance. Should the Examiner believe that a telephonic interview would expedite prosecution, she is invited to call the undersigned attorney at the address provided below.

Respectfully submitted,



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Enclosure: Patent 6,183,959
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